EXECUTIVE SUMMARY

The United States Environmental Protection Agency (U.S. EPA), Office of Pollution Prevention and Toxics (OPPT), identified and chose trichloroethylene (TCE) for risk evaluation as part of its Existing Chemicals Management Program under the Toxics Substances Control Act (TSCA).

TCE is a volatile organic compound (VOC) that is classified as a human carcinogen. Its consumption in the U.S. is 255 million pounds (lbs) per year. TCE is widely used in industrial and commercial processes, and also has some limited uses in consumer products.

Main Conclusions of this Risk Assessment

This risk assessment identifies cancer risk concerns and short-term and long-term non-cancer risks for workers and occupational bystanders at small commercial degreasing facilities and dry cleaning facilities that use TCE-based solvents and spotting agents, respectively.

EPA/OPPT also identifies short-term non-cancer risks for consumers and residential bystanders from the use of TCE-containing solvent degreasers and spray-applied protective coatings.

The Focus of this Risk Assessment

This assessment characterizes human health risks from inhalation exposures to TCE for the following uses:

1. Commercial use of TCE as a solvent degreaser
2. Consumer use of TCE as a solvent degreaser
3. Consumer use of TCE as a spray-applied protective coating for arts and crafts
4. Commercial use of TCE as a spotting agent at dry-cleaning facilities

EPA/OPPT selected these uses because they were expected to make frequent use of TCE in high concentrations and/or pose high potential for human exposure. Additional information is provided in the risk assessment regarding the criteria for inclusion of uses and the various assumptions in applying these criteria.

The main route of exposure for TCE is believed to be inhalation for the uses identified in this assessment. EPA/OPPT recognizes that highly volatile compounds such as TCE may also be absorbed through the skin. However, based on the physical-chemical properties of TCE and the scenarios described in this assessment, EPA/OPPT believes that inhalation is the main exposure pathway for this risk assessment. Recent modeled and experimental work supports this assumption that inhalation is the predominant exposure pathway (see Section 1.3.2). This assessment may underestimate total exposures resulting from the uses of TCE due to this assumption.

This risk assessment does not include an assessment of environmental effects. Based on TCE's moderate persistence, low bioaccumulation, and low hazard for aquatic toxicity, potential environmental impacts are judged to be low for the environmental releases associated to the TSCA uses under the scope of this risk assessment. That judgment should not be misinterpreted as saying that the fate and transport properties of TCE suggest that water and soil contamination is likely low or do not pose an environmental concern. In fact, EPA's Office of Solid Waste and Emergency Response and the EPA Regions are addressing TCE contamination in groundwater and contaminated soils at large number of sites. While the primary concern with this contamination has been human health, there is potential for TCE exposures to ecological receptors in some cases.

Human Populations Targeted in This Assessment

EPA/OPPT assessed acute and chronic risks for workers at small degreasing facilities and dry cleaning facilities that may use TCE as a solvent degreaser or spotting agent, respectively. EPA/OPPT assumes that workers at these small degreasing and dry cleaning facilities would be adults of both sexes (≥16 and older, including pregnant women) based upon occupational work permits, although exposures to younger individuals may be possible in occupational settings. Risks are also estimated for occupational bystanders, who are assumed to be workers in the vicinity of the degreasing and spotting operations, but not actually performing the operation.

EPA/OPPT also examined acute risks for consumer exposures in residential settings. EPA/OPPT assumes that consumers would be individuals that intermittently use TCE in and around their homes, whereas bystanders would be individuals physically close to the use activity but not using the product. EPA/OPPT assumes that consumer users would generally be adults of both sexes (≥16 and older, including pregnant women), although exposures to teenagers and even younger individuals may be possible in residential settings. However, risk estimates are focused on the most susceptible life stage, which are pregnant women and their developing fetus. This focus is supported by the hazard findings in the TCE IRIS assessment, which conclude that developmental toxicity is the most sensitive health effect associated to TCE exposure (EPA, 2011e).

Workplace Exposures at Commercial Degreasing and Dry Cleaning Facilities

In order to estimate TCE emissions in the workplace, EPA/OPPT used readily available information from the National Emissions Inventory (NEI), the Toxics Release Inventory (TRI), and a study on the use of spotting chemicals prepared for the California EPA and EPA Region 9 (CalEPA/EPA, 2007). To estimate workplace exposures, these emission estimates were incorporated into a Near Field/Far Field (NF/FF) mass balance model.

It is important to note that the NF/FF model has been extensively peer-reviewed, is extensively used, and results of the model have been compared with measured data. The comparison indicated that model and measured values agreed to within a factor of about three (Jayjock et al., 2011). In estimating workplace exposures, EPA/OPPT assessed various exposure scenarios.

For example, engineering controls such as local exhaust ventilation (LEV) were taken into account.

Although relevant exposure monitoring data are limited, EPA/OPPT did identify monitoring data from the Occupational Safety and Health Administration (OSHA)(Coble, 2013) and site-specific data from the National Institute for Occupational Safety and Health (NIOSH)(NIOSH, 1997b). The exposure estimates (with and without LEV) were of the same order of magnitude as measured values:

1. For commercial degreasing facilities, EPA's exposure estimate ranged from 0.04 to 197 parts per million (ppm); measured data from OSHA ranged from 0.06 to 380 ppm.
2. For dry cleaning facilities, EPA's site-specific exposure estimate ranged from 0.8 to 2.1 ppm; measured data reported by NIOSH ranged from 2.37 to 3.11 ppm.

Consumer Exposures from Solvent Degreasing and Spray-Applied Coatings

EPA/OPPT used the Exposure and Fate Assessment Screening Tool Version 2 (E-FAST2) /Consumer Exposure Module (CEM) (EPA, 2007b) to estimate TCE exposures for the consumer use scenarios. This modeling approach was selected because emissions and monitoring data were not available for the TCE uses under consideration.

The model used a two-zone representation of a house to calculate the TCE exposure levels for consumers and bystanders. The modeling approach integrated assumptions and input parameters about the chemical emission rate over time, the volume of the house and the room of use, the air exchange rate and interzonal airflow rate. The model also considered the exposed individual's locations, body weights and inhalation rates during and after the product use (EPA, 2007b).

The high-end inhalation exposure estimates for the consumer scenarios were as follows:

1. 0.4 ppm for users of TCE-containing clear protective coating sprays
2. 0.1 ppm for bystanders of TCE-containing clear protective coating sprays
3. 2 ppm for users of TCE-containing solvent degreasers
4. 0.8 ppm for bystanders of TCE-containing solvent degreasers

Characterization of Hazards and Risks to Human Health

The assessment uses the hazard and dose-response information published in the final toxicological review that the U.S. EPA's Integrated Risk Information System (IRIS) published in 2011 (EPA, 2011e). The TCE IRIS assessment used a weight-of-evidence approach, the latest scientific information and physiologically-based pharmacokinetic (PBPK) modeling to develop hazard and dose-response assessments for TCE's carcinogenic and non-carcinogenic health effects resulting from lifetime inhalation and oral exposures. In addition to relying on the latest scientific information, the TCE IRIS assessment underwent several levels of peer review including agency review, science consultation on the draft assessment with other federal agencies and the Executive Office of the President, public comment, external peer review by

the EPA's Science Advisory Board (SAB) in 2002, scientific consultation by the U.S. National Academy of Sciences (NAS) in 2006, external peer review of the revised draft assessment by the EPA's Science Advisory Board (SAB) in January 2011, followed by final internal agency review and EPA-led science discussion on the final draft.

TCE's Carcinogenic Hazards and Risks:

TCE is carcinogenic to humans by all routes of exposure as documented in the TCE IRIS assessment. This conclusion is based on strong cancer epidemiological data that reported an association between TCE exposure and the onset of various cancers, primarily in the kidney, liver and the immune system (i.e., non-Hodgkin lymphoma or NHL) (EPA, 2011e). Further support for TCE's carcinogenic characterization comes from (1) positive results in multiple rodent cancer bioassays in rats and mice of both sexes, (2) similar toxicokinetics between rodents and humans, (3) mechanistic data supporting a mutagenic mode of action for kidney tumors, and (4) the lack of mechanistic data supporting the conclusion that any of the mode(s) of action for TCE-induced rodent tumors are irrelevant to humans (EPA, 2011e). Additional support comes from the recent evaluation of TCE's carcinogenic effects by the International Agency for Research on Cancer (IARC). IARC (2014) classifies TCE as carcinogenic to humans (Group 1).

EPA/OPPT used the inhalation unit risk (IUR) of 2×10^{-2} per ppm (4×10^{-6} per $\mu g/m^3$) reported in the TCE IRIS assessment to estimate excess cancer risks for the occupational scenarios. The IUR is the estimated upper bound excess lifetime cancer risk resulting from continuous exposure to an airborne agent at 1 $\mu g/m^3$ (EPA, 2011b). The IUR for TCE is based on human kidney cancer risks and adjusted for potential risks for NHL and liver cancer based on human epidemiological data (EPA, 2011e). There is high confidence in the IUR because it is based on good quality human data and it is similar to unit risk estimates derived from multiple rodent bioassays (EPA, 2011e). Moreover, there is sufficient weight of evidence to conclude that TCE operates through a mutagenic mode of action for kidney tumors, which supports the linear extrapolation approach (EPA, 2011e).

TCE's Non-Carcinogenic Hazards and Risks:

TCE exposure is associated with a range of non-cancer health effects in humans and animals. Non-cancer risks for the various exposure scenarios were evaluated using the dose-response information reported in the TCE IRIS assessment (EPA, 2011e). The TCE IRIS assessment used physiologically-based pharmacokinetic (PBPK) modeling to estimate hazard values (i.e., human equivalent concentrations or HECs) indicative of adverse health effects representing six health effects domains: kidney, liver, immunotoxicity, neurotoxicity, reproductive toxicity, and developmental toxicity.

Different health endpoints were used to evaluate risks based on the expected durations of exposure in the scenarios considered in this assessment. For instance, both acute and chronic health effects endpoints were used for the occupational scenarios (i.e., small commercial degreasers and spot cleaning workers and bystanders). In that case, a variety of health effects

endpoints were used to evaluate repeated (chronic) exposures to TCE (i.e., toxicity to the liver, kidney, nervous system, immune system, the reproductive system, and developmental toxicity). For the consumer use scenarios, developmental toxicity endpoints were used to assess risks for acute exposures.

EPA/OPPT used developmental endpoints for the acute risk assessment based on U.S. EPA's policy that a single exposure of a chemical within a critical window of fetal development may produce adverse developmental effects (EPA, 1991). Particularly, this assessment used the PBPK-derived HECs reported for developmental animal studies reporting fetal cardiac defects. TCE-induced fetal cardiac malformations are biologically plausible based on the weight of evidence analysis presented in the TCE IRIS assessment, which considered human and animal findings as well as mechanistic data.

These hazard values were expressed as HECs at the 50^{th}, 95^{th} or 99^{th} percentile of the combined uncertainty and variability distribution of human internal doses, as estimated by the TCE PBPK model (EPA, 2011e). The HEC_{95} and HEC_{99} were defined as the concentrations of TCE in air for which there is 95% and 99% likelihood, respectively, that a randomly selected individual would have an internal dose less than or equal to the internal dose of the hazard value. On the other hand, the HEC_{50} was defined as the concentration of TCE in air for which there is a 50% likelihood that a randomly selected individual would have an internal dose less than or equal to the internal dose of the hazard value (EPA, 2011e). The TCE IRIS assessment preferred the HEC_{99} for the non-cancer dose-response derivations because the HEC_{99} was interpreted to be protective for a sensitive individual. EPA/OPPT supported the interpretation of the HEC_{99} as expressed in the TCE IRIS assessment. Hence, HEC_{99}-based risk estimates are favored in this assessment over those estimated from the HEC_{50} and HEC_{95} values, but risk estimates for all of the HEC percentiles were presented to provide a sense of the variability in the risk estimates.

EPA/OPPT used margin of exposures (MOEs) to estimate non-cancer risks based on (1) the lowest PBPK-derived HECs within each health effects domain reported in the TCE IRIS assessment; (2) the same endpoint/study-specific uncertainty factors (UFs) that the IRIS program applied to the PBPK-derived HECs; and (3) the exposure estimates calculated for the TCE uses examined in this risk assessment. MOEs allowed us to have a better picture of the non-cancer risk profile of TCE by presenting a range of risk estimates for different non-cancer health effects for different exposure scenarios.

Uncertainties of this Risk Assessment

As with any risk assessment, there are uncertainties that need to be considered when interpreting the results. Assumptions were used in estimating the occupational and consumer exposure scenarios covered in this assessment. In addition, there are uncertainties in the hazard/dose-response and risk characterization assessments. EPA/OPPT discusses these uncertainties qualitatively and recognizes that they may under- or over-estimate actual risks.

The Results of this Risk Assessment

Size of the Exposed Population

- Approximately 30,000 workers and occupational bystanders at small commercial degreasing operations.
- Approximately 300,000 workers and occupational bystanders at dry cleaning operations.
- No data were available to estimate the number of consumers and bystanders exposed to TCE during the use of degreasers and arts/crafts clear protective coating spray.

Cancer Risks:

- There are cancer risk concerns for users and bystanders occupationally exposed to TCE when using TCE-containing vapor degreasers and spot cleaners in small commercial shops and dry cleaning facilities, respectively.
- Many of the commercial vapor degreasing and spot cleaning exposure scenarios exceed the excess lifetime cancer risk probabilities of 1 chance in 10,000, 100,000 or 1 million (i.e., target cancer risks of 10^{-4}, 10^{-5} and 10^{-6}, respectively) of an individual developing cancer.
- The occupational exposures to commercial degreasers show the greatest cancer risk when compared to the spot cleaning exposure scenarios.

Acute Non-Cancer Risks:

- There are acute non-cancer risks for developmental effects (i.e., cardiac defects) for most occupational and residential exposure scenarios (i.e., MOEs were below the benchmark MOE of 10).
- The commercial vapor degreasing and consumer spray degreasing exposure scenarios show greater acute risks for developmental effects than those reported for the spot cleaning exposure scenarios.

Chronic Non-Cancer Risks:

- There are chronic non-cancer risks for a range of human health effects in both the occupational degreaser and spot cleaning exposure scenarios (i.e., MOEs were below the benchmark MOE).
- The greatest concern is for developmental effects (i.e., fetal cardiac defects), followed by kidney effects and then immunotoxicity, with an overall higher chronic risk for the degreaser exposure scenarios. In general, this concern is present for lower and upper-end exposures and in the presence or absence of room ventilation (LEV vs. no LEV).
- There are chronic risks for reproductive effects and neurotoxicity for degreaser worker exposure scenarios and most of the degreaser bystander exposure scenarios. However, the risks concern for these effects are reported for fewer spot cleaning worker and bystander scenarios, and are generally attributed to exposure conditions without room ventilation.
- There are chronic risks for liver effects although the risks were less prominent than those reported for other health effects. These risks were found only in the degreaser worker and

bystander exposure worst case scenarios, and the spot cleaning worker and bystander worst case scenarios with no LEV.